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EXAMINER

CLOW, LORI A

ART UNIT PAPER NUMBER

1631

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/744,628

Applicant(s)

YIP ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 23 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 3,6,8-15 and 20-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3,6,8-15 and 20-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Applicants' arguments, filed 23 February 2004, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 3, 6, 8-15, and 20-22 are currently pending.

The Examiner would like to thank Applicant for providing a clear copy of previously filed Amendment B, filed 28 July 2003.

The claim objection to the term "IR" has been withdrawn in view of Applicant's amendments.

The 112, 1<sup>st</sup> paragraph new matter rejection over claim 19 has been withdrawn in view of Applicant's amendments.

### **Information Disclosure Statement**

The Information Disclosure Statement filed 19 March 2004 has not been considered at this time. Due to the transition from paper files to electronic files, the IDS may have been lost. Applicant is requested to kindly re-submit the IDS and references.

### **Claim Objections**

Claims 3 and 9 are objected to for reciting "Table I". The specification contains only a "Table 1". Correction is requested.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 6, 8-15, and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a new grounds of rejection.*

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) and e) In order to practice the claimed invention one of skill in the art must be able to determine whether or not a compound modulates insulin receptor activity. However, the methods of claims 3, 6, 8-15, and 20-22 are not enabled as the claims are lacking critical steps and information required for the performance of said methods. One of skill in the art would not be able to perform the invention as claimed and the steps as presently recited would not result in

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obtaining the desired information from the methods, i.e. prediction of modulators of insulin activity from a fitting method.

In claim 3 and dependent claims, the method to supposedly determine a modulator of insulin activity comprises steps of comparing the structure of a compound to the fitted quaternary structure of the insulin receptor to determine if the compound interacts with the receptor. The additional steps include providing a computer program with structural coordinates such that the program displays a structure of the ligand, comparing structural coordinates of a compound and ligand and determining whether the compound fits spatially into the ligand binding site and is capable of changing insulin receptor from inactive conformation to an active conformation or biasing insulin receptor toward an active conformation.

Just because a compound may fit into a site on the insulin receptor does not mean that it will in any way have an effect on receptor activity. A simple comparison of structure to a compound would not yield any information regarding insulin receptor activity unless subsequent steps to test the fitting of the compound with the receptor were performed such that the steps exemplified how to determine the change in conformation. There is no indication in the specification that binding will necessarily change conformation. How does one determine whether the compound is capable of changing the receptor from active to inactive without performing another step, such as an assay? Is the determination a virtual determination based upon a threshold value that may indicate probable change in conformation? Without indication in the specification for what indicates conformational change of the receptor, the claims are not enabled.

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Further, claims 11-15 still recite the further steps of providing a computer program on the computer, the computer program including structural coordinates including at least one residue from the Cam-loop segment [...]. There is no indication or guidance in the specification about the nature or meaning of a “cam”. Applicant has amended the claims to recite only “Cam-loop segment”, however, the nature of this segment is still not defined. There are specific residues indicated as Cam-loop segment in Table 2, however, there is nothing stating that these residues are, in fact, the definition of a Cam-loop. Are these the only residues in a Cam-loop (see 112, 2<sup>nd</sup> paragraph rejection). As such, one of skill in the art would not know how to use this information to perform the steps of the invention.

One would look to the art to practice the invention. However, the art describes determining modulators of activity either by in vivo and in vitro assays or by computer simulation, as in the present invention. The prior art, however, provides specific steps that would lead one to identify modulators of activity. For example, the CAVEAT program (Lauri et al. Journal of Computer-Aided Molecular Design (1994) Vol. 8, pages 51-66) is described in great detail such that molecules and structures are analyzed by energy conformations, structures with patterns, steric interactions, rank, etc. such that mimics, or modulators may be determined. However, is not possible to practice said invention without undue experimentation due to the lack of method steps that would enable one to determine a modulator of activity from a mere comparison.

b) and c) The specification provides a working example at pages 59-60. However, there is nothing to indicate how the activation or inactivation of the receptor is measured.

d) The invention is drawn to determining modulators of the insulin receptor.

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f) The skill of those in the art of pharmacogenomics is high.

g) The art is predictable if the proper method steps are employed.

h) The claims are broad because they are drawn to methods without sufficient steps to perform the methods. The skilled practitioner would first turn to the instant specification for guidance to practice the claimed methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art does not teach these methods. Finally, said practitioner would turn to trial and error experimentation to determine the limits and steps required. Such represents undue experimentation.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-15, 21, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11, 13, and dependent claims recite "Cam-loop segment". It is unclear how this is defined. Applicant has pointed to Table 2 as the definition of Cam-loop segment. Table 2 lists specific amino acid residues under the heading of Cam-loop segment. However, it is unclear from the specification if these are the only residues in the Cam-loop segment or are there other residues that make up the segment. Cam-loop segment is not defined as a particular domain with

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any particular activity. Further, claim 13 still includes “defining a cam loop conformation”, which is not defined in the specification. What is a cam loop conformation?

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (571) 272-0549.

MARJORIE MORAN  
PATENT EXAMINER

*Marjorie A. Moran*  
5/13/04

May 13, 2004

Lori A. Clow, Ph.D.

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*Lori A. Clow*